

## **REMARKS**

### **1. Status of the Claims**

The independent claims have been amended to define that the “host cell” is a “plant cell”. This amendment is supported by, for example, original claim 14.

The independent claims have also been amended to define that the modified immunoglobulin heavy chain is co-expressed with a light chain. This amendment is supported by the specification at, for example, the penultimate paragraph on page 4 of the specification.

As a result, the amendments to the claims do not in any way attempt to enter new matter.

### **2. Overview of the Rejections**

It is noted with appreciation that several of the previous rejections have been indicated as being withdrawn on pages 2-4 of the Office Action. However, the Examiner has maintained the rejections of the claims for alleged lack of written description, alleged lack of enablement and obviousness. These rejections are substantially the same as originally set forth in the Office Action of June 21, 2007. But in the meantime, Applicants have submitted significant Declaration evidence to directly address all of the points raised by the Examiner in the written description, enablement and obviousness rejections. Further Declaration evidence, as discussed below is submitted with the present response. The Examiner, on the other hand, has not rebutted Applicants’ arguments and evidence with any counter evidence. Applicants submit that, as a result, the preponderance of evidence clearly supports the Applicants’ position that the claims fully comply with the enablement and written description requirements of 35 U.S.C. § 112 and that the claims define non-obvious patentable subject matter. It is simply improper for the Examiner to remain fixed on positions of patentability without giving due consideration and weight to Applicants’ evidence, and without even attempting to counter Applicants’ evidence with counter evidence.

The Examiner is reminded that “patentability determinations are based on a preponderance of the evidence. ‘After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of the evidence with due consideration to persuasiveness of argument’.” (*Ex parte Rutanen*, at page 8, Appeal 2009-001910 (USPTO Bd. Pat. App. & Int., August 4, 2009); citing *In re Oetiker*, 977 F2d 1442, 1445 (Fed. Cir. 1992)). A copy of the decision in *Ex parte Rutanen* is enclosed as Exhibit 1. (The Examiner will note that the *Ex parte Rutanen* decision was subsequently withdrawn because of procedural steps by the Applicant, but the reasoning of the Board is still valid and applicable to the present case).

### **3. Claim Rejections - 35 U.S.C. § 112 - Enablement**

Claims 1, 34-38, 40-44, 46, 48, 50, 52, 82-86 and 88-89 have been rejected for alleged lack of enablement. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

One basis for the Examiner’s rejection is the position that the claims lack enablement “for expressing a functional antibody having only a heavy chain.” (See page 9 of the Office Action). In response thereto, as noted above, the independent claims have been amended to recite that the modified heavy chain is co-expressed with a light chain. Although the Applicants do not concede the propriety of the Examiner’s rejection on this point, it is believed that this basis for the objection has been obviated by the amendment to the claims.

With respect to the remaining positions set forth in the Examiner’s enablement rejection, attention is directed to the enclosed Declaration of Dr. Frigerio, dated 9 September 2009 (Exhibit 2, hereinafter “the Frigerio II Declaration”). Paragraphs 5-17 of the Declaration specifically address the various points raised by the Examiner in the enablement rejection. The arguments and positions set forth in the Frigerio II Declaration will explain why one skilled in the art could

indeed practice the full scope of the present claims based upon the teachings of the present application and the knowledge of those skilled in the art at the time of filing the present application, so those arguments will not be reiterated herein. As noted in paragraph 11 of the Frigerio II Declaration, the enclosed flow diagram (Exhibit A) summarizes the procedures described in the present application for making antibodies according to the claimed method and paragraphs 12-16 of the Frigerio II Declaration further explain how one skilled in the art following those procedures could practice the full scope of the claimed invention.

In addition, paragraph 17 of the Frigerio II Declaration describes how additional constructs according to the present invention were successfully prepared without any undue experimentation.

The Examiner is reminded that Applicants also submitted a Declaration by Dr. Vitale on October 31, 2007 which, in paragraph 4, further explained how one skilled in the art as of the date of the present application could have practiced the full scope of the present invention.

Applicants submit that the preponderance of the evidence clearly establishes that the present claims are indeed enabled, and that the Examiner's rejections should be withdrawn.

#### **4. Claim Rejections Under 35 U.S.C. § 112 - Written Description**

Claims 1, 34-38, 40-44, 46, 48, 50, 52 and 82-87 have been rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of compliance with the written description requirement. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The fundamental basis for the Examiner's continued rejection is the allegation that the specification does not describe "a reasonable number of antibody embodiments falling within the scope" of the claims. (See page 6 of the Office Action). As with the enablement rejection, Applicants submit that the Examiner has improperly maintained the rejection without giving due

consideration of Applicants' previously submitted evidence. The previously submitted Vitale Declaration at paragraph 4 specifically explains why one skilled in the art would indeed understand that the Applicants were in possession of the claimed invention at the time of the present application.

The Examiner is again referred to the enclosed recent decision in *Ex parte Rutanen* (at page 4) and the reminder therein to the Examiner of the basic principle underlying the written description requirement as follows:

“The ‘written description’ requirement...serves both to satisfy the inventor’s obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed.... The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence.” *Capon v. Eshhar*, 418 F3d 1349 (Fed. Cir. 2005). “It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention.” *Id.* at 1359.

Applicants have appropriately responded to the Examiner’s rejection by providing Declaration evidence in which Dr. Vitale specifically states that the specification as filed “provides a sufficient number of representative species of sequences to demonstrate that the invention works across the whole claim genus of sequences” (see paragraph 4 of the Vitale Declaration). Applicants submit that the Examiner’s continued rejection in the face of evidence again fails to evaluate patentability based upon the preponderance of the evidence. Applicants submit that proper evaluation of the evidence requires that the rejection be withdrawn.

## **5. Claim Rejections - 35 U.S.C. § 103**

Claims 1, 34, 35, 38, 40, 41, 46, 48 and 50 have been rejected under 35 U.S.C. § 103 over *Frigerio et al.* in view of *Vitale* and *Raikhel, Klide et al.* and *Matsuoka et al.* This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

First of all, it is noted that claim 88 has not been rejected over the prior art. Thus, the Examiner apparently recognizes that the modification recited in claim 88 specifically directed to “deleting the last 16 amino acids of the immunoglobulin heavy chain molecule” is not taught or suggested in the prior art.

With respect to the other claims, Applicants submit that the Examiner has utterly failed to identify any portion of any prior art reference that allegedly teaches or suggests step (b) of Applicants’ independent claims. Pages 15 and 16 of the outstanding Office Action set forth the Examiner’s attempt to summarize and combine the teachings of the cited references. But missing from the Examiner’s discussion is any citation to some portion of one of the cited references that actually teaches step (b) of Applicants’ independent claims, namely the step of modifying the nucleotide sequence in the region of the sequence encoding the c-terminus 18 amino acids of the immunoglobulin heavy chain molecule.

It is well established that “obviousness requires a suggestion of all limitations in a claim”. *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F3d. 1333, 1342 (Fed. Cir. 2003). This requirement still applies in the “post-KSR era” because even the Supreme Court in *KSR* emphasized that “there must be some articulated reasoning with some rational underpinning to support the legal inclusion of obviousness”. *Ex part Baldenisu et al.*, page 7, Appeal 2007-2604, January 15, 2008 (Exhibit 3), citing *KSR Int’l v. Teleflex Inc.* 127 S. Ct. 1727, 1741 (2007).

Applicants have previously submitted evidence to counter the Examiner’s obviousness rejection. Attention is again directed to the Vitale Declaration at paragraph 5, and to the Figerio I Declaration submitted on October 31, 2007. Attention is also directed to the new Frigerio II Declaration, where at paragraph 18 Dr. Frigerio further addresses why one skilled in the art would not look for vacuolar sorting signals in antibodies, so that the present invention would not have been obvious to one of ordinary skill in the art.

In view of the above, Applicants submit that all of the Examiner's rejections have been rebutted and countered with evidence, such that the preponderance of the evidence clearly weighs in favor of patentability of the claims. Reconsideration and withdrawal of all the rejections are, therefore, requested.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a three (3) month extension of time for filing a reply in connection with the present application, and the required fee of \$555.00 is attached hereto.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson Reg. No. 30,330 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

By 

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